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Adv Parasitol. Author manuscript; available in PMC 2011 October 19.

Published in final edited form as:
Adv Parasitol. 2000 ; 47: 309–330.

Forecasting Disease Risk for Increased Epidemic Preparedness in Public Health

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Abstract

Emerging infectious diseases pose a growing threat to human populations. Many of the world's epidemic diseases (particularly those transmitted by intermediate hosts) are known to be highly sensitive to long-term changes in climate and short-term fluctuations in the weather. The application of environmental data to the study of disease offers the capability to demonstrate vector–environment relationships and potentially forecast the risk of disease outbreaks or epidemics. Accurate disease forecasting models would markedly improve epidemic prevention and control capabilities. This chapter examines the potential for epidemic forecasting and discusses the issues associated with the development of global networks for surveillance and prediction. Existing global systems for epidemic preparedness focus on disease surveillance using either expert knowledge or statistical modelling of disease activity and thresholds to identify times and areas of risk. Predictive health information systems would use monitored environmental variables, linked to a disease system, to be observed and provide prior information of outbreaks. The components and varieties of forecasting systems are discussed with selected examples, along with issues relating to further development.

1. INTRODUCTION

Environmental change, human demography, international travel, microbial evolution and the breakdown of public health facilities have all contributed to the changing spectrum of infectious diseases with which the global community is challenged (Bryan *et al.*, 1994). Existing mechanisms for infectious disease surveillance and response are inadequate to meet the increasing needs for prevention, detection, reporting and response (CDC, 1994; CISET, 1995). The ability to predict epidemics will provide a mechanism for governments and health-care services to respond to outbreaks in a timely fashion, enabling the impact to be minimized and limited resources to be saved (LaPorte, 1993; Wilson, 1994). For many infectious diseases, particularly those transmitted by arthropod vectors, advanced surveillance and modelling technologies incorporating environmental data create the potential to predict the temporal and spatial risk of epidemics. When combined with communication technologies, these techniques can provide important tools that are both cost-effective and timely (Susser and Susser, 1996). As disease boundaries shift and expand to threaten new populations, there is increasing need to develop operational models with

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predictive capacity: ‘As more experience is gained in linking changes detected by global imaging with changes in disease patterns, geographical information systems are likely to play an increasingly important role in forecasting outbreaks, especially those of vector-borne diseases such as malaria’ (Greenwood, 1998).

Advances in disease surveillance systems, epidemiological modelling and information technology have generated the expectation that early warning systems are not only feasible but necessary tools to combat the re-emergence and spread of infectious diseases. While many of the environmental data used in these systems are available free or at low cost, the quality and availability of epidemiological data vary enormously. The length and spatial extent of the epidemiological data series are particularly important for investigating annual and inter-annual patterns of disease. Elsewhere in this volume the evolution of remote sensing instrumentation (Hay, this volume) and the application of satellite data to problems of disease risk prediction are reviewed and discussed (Rogers, this volume; Hay *et al.*, this volume; Randolph, this volume; Brooker and Michael, this volume) and will not be reiterated here. This chapter focuses particularly on techniques being developed with the view to predicting diseases in both time and space. Figure 1 illustrates the terminology that is used in this chapter. Briefly, surveillance and early detection refer to the monitoring of reported case data; disease forecasting is a medium term warning of suitable conditions for a disease (e.g. increased rainfall for malaria); epidemic warning and prediction are more short-term indications of risk with more specificity in time and space.

2. DISEASE FORECASTING

2.1. Historical Early Warning Systems

Efforts to use environmental data for epidemic prediction and response began in the early 1920s in India, when nearly half a century of meteorological data and 30 years of records of tropical diseases had been amassed by province and district (Rogers, 1925a). Risk maps were developed by combining meteorological and health records for diseases such as leprosy (Rogers, 1923), pneumonia (Rogers, 1925b) and smallpox (Rogers, 1926). These maps offered predictions with a 2–3 month lead-time to allow government response. Gill (1921) was also able to link rainfall and river flooding to subsequent outbreaks of malaria. Further work by Gill (1923) used rainfall and a series of health and demographic inputs to establish 4-month and 2-month malaria predictive warnings for two decades in the various districts of the Punjab, until the province ceased to exist with the partitioning of India in 1947. Swaroop (1949) provides an excellent review of these investigations.

2.2. The Components of an Early Warning System

A framework for early warning systems (EWSs) for epidemic preparedness was developed in the mid-1980s, during the collaborative efforts to design and build EWSs for famine prediction in Africa (Walsh, 1988). Davies *et al.* (1991) defined an EWS for famine as:

> a system of data collection to monitor people’s access to food, in order to provide timely notice when a food crisis threatens and thus to elicit appropriate responses.

Reviews of these based on remote sensing operational famine EWSs can be found in Hutchinson (1991) and Hielkema and Snijders (1994). Early warning for epidemics refers to risk formulation or modelled projections of potential outbreaks based on systematically collected information from the monitored site(s) to allow appropriate and timely actions for mitigation and response.

There are three components of an EWS. These are (1) routine surveillance of the targeted disease; (2) modelling the disease risk based on historical surveillance and contemporary environmental data; and (3) forecasting future risk through the use of predictive models and

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continued epidemiological and environmental surveillance. During the 1990s, technological advances have made disease EWSs more feasible. These include the development and global penetration of the Internet (Valleron *et al.*, 1986), online electronic communication between health care providers and epidemiologists (CISET, 1995), and improvements in satellite imaging that allow improved environmental characterization of sentinel sites (Hay *et al.*, 1996; Hay and Lennon, 1999; Goetz *et al.*, this volume). We acknowledge the obvious challenge to make such technological developments available to all.

2.2.1. Component 1: Disease Surveillance—A sentinel network is an interactive disease surveillance system that involves the collection of health data on a routine basis, usually by health care professionals over a wide (usually country level) area (Valleron *et al.*, 1986; Girard, 1997; Fourquet and Drucker, 1997). In most industrialized nations, notification of many infectious diseases is a statutory requirement. Rapid collection of data and assessment of regional and national statistics leads to early detection of changes in the incidence of infections (CDC, 1994; Greenwood, 1998; Heymann and Rodier, 1998). The database also provides information for the planning and implementation of intervention(Choi, 1998; Kafadar and Stroup, 1992). The growth of such sentinel systems, from independent national networks to co-ordinated international information systems, has generated a demand for health information systems capable of forecasting disease (Flahault *et al.*, 1998; Nabarro and Tayler, 1998).

When teleinformatics was introduced into public health fields the potential for its use as a rapid and early warning system soon became evident. France developed its sentinel system (Valleron *et al.*, 1986; Fourquet and Drucker, 1997), New York State implemented Healthcom, and the Center for Disease Control (CDC) set up an electronic network between the various US states' Departments of Health. As data were collected it became possible to identify evolving temporal and spatial patterns, such as growing or lessening risks of reported diseases, seasonality, clustering, and so on. This spawned a huge literature on detection of anomalies in disease surveillance data (for example, Zeng *et al.*, 1988; Stroup *et al.*, 1989; Watier *et al.*, 1991; Frisén, 1992; Nobre and Stroup, 1994; Stern and Lightfood, 1999; Vanbrackle and Williamson, 1999).

Increasingly powerful platforms for data collection and manipulation developed alongside these information networks. Relational databases were undergoing rapid evolution, permitting manipulation and analysis of huge fluxes of information. Client–server architecture developments also provided for more rapid remote access, allowing multiple simultaneous sessions to be open on a unique application for analysts and data providers. For the first time it became possible not only to provide baseline health statistics in near real time, but also to archive and mine the data electronically and to add additional information from other sources. Profiles of the outbreak and spread of a disease could also be created quickly enough so that the information could be returned to public health organizations charged with containing the disease, increasing their ability to respond. This led to the present understanding that a facility-based sentinel surveillance system can play an important role in providing information for monitoring communicable diseases, guiding further investigation, evaluating control measures, and predicting epidemics (Berkelman, 1994, 1998; Shalala, 1998). Some of the epidemiological insights that can be drawn from the archival and systematic long-term collection of disease data are identified by Cliff *et al.* (1998).

(a) The French Sentinel System: France took a technological lead in electronic disease surveillance, with a national telecommunications programme instituted in 1983 that provided videotext home terminals free of charge to French citizens. In 1984, the Institut National de la Santé et de la Recherche Médicale (INSERM), in collaboration with the

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Ministry of Health, initiated a program to provide for electronic monitoring of communicable diseases. Today, a volunteer sample of about 1% of French general practitioners (GPs) remotely enters reports on several diseases on a weekly basis (Flauhault *et al.*, 1998). This system is the basis for one of the largest databases of individual cases (including time-to-onset and geographical location) of diseases such as influenza-like illness, acute diarrhoea and chickenpox. Bonabeau *et al.* (1998) demonstrate some of the detailed insights into the geographical spread of disease that can be derived from such large databases. The contemporaneous systems of the United States' Centers for Disease Control (CDC) in Atlanta, as well as the Royal College of GPs in the UK, still used a system based on index cards.

(b) The US Surveillance System: In the United States, individual states determine which diseases are reported internally, and together determine which diseases will be reported to the federal government on a voluntary countrywide basis (Berkelman, 1998). Currently, all states use a standardized weekly form submitted by e-mail to the CDC on the National Electronic Telecommunications System for Surveillance (NETSS). In return, the CDC established the Public Health Network (PHNET), a tool to return information alerts to state departments of health (SHD) (Halperin *et al.*, 1992). For a long time, this system was based on an electronic text-message system of the Morbidity and Mortality Weekly Report (MMWR) which SHDs received earlier than other subscribers. Currently, using the graphic capabilities of the Internet, up-to date maps and graphs are now increasingly available.

(c) Development of a Global Network for Disease Surveillance: Other sentinel systems have been set up in Europe (Snacken *et al.*, 1992, 1998; Szecsenyi *et al.*, 1995; Fleming and Cohen, 1996; Gylys *et al.*, 1998). Following the establishment and operation of national surveillance systems, international cooperation is resulting in the development of global surveillance systems for targeted diseases. Working through the trans-Atlantic Agenda, the US and the European Union (EU) are negotiating to share surveillance data on a variety of diseases (Berkelman, 1998; Heyman and Rodier, 1998). Collaborative surveillance efforts also exist between US agencies and the World Health Organization (WHO) for the establishment of regional centres for monitoring disease as well as for improving communications infrastructure for future efforts (Shalala, 1998).

2.2.2. Component 2: Developing a Model—Disease forecasting involves modelling, which may be based either on statistical relationships established between past case numbers and environmental predictors (the 'statistical approach'), or on sets of equations that attempt to capture the biology of the transmission processes (the 'biological approach'), both reviewed by Rogers (this volume). Briefly, the statistical approach requires samples from as wide a range of environmental conditions as possible: predictions arising from this approach assume that the future will be the same as the past, i.e. that the relationships already established between case numbers and environmental variables will persist into the future. The biological approach requires details on all the parameters and variables considered to be important in transmission (these may sometimes be estimated by *post hoc* analysis of disease data sets): predictions arising from this approach are in theory able to incorporate the effects of environmental changes, or interventions, as long as the impacts of each of these changes on the key transmission parameters are established.

It should follow from the above that in the absence of full knowledge of all the transmission pathways for any particular diseases, only the statistical approach is possible. This explains why much of the early epidemiology of poorly-understood diseases such as cancer adopted the statistical route. Statistical models can be extremely powerful, but should be only a temporary substitute for the biological process-based models, whose development exposes

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our full ignorance of the systems we study. It is only by addressing this ignorance that real progress will be made.

There is, however, an important dilemma in the statistical/biological model debate. It seems likely that case numbers in many diseases arise from a combination of factors, some of which are intrinsic to the disease and its various hosts and others which are extrinsic, or environmental. The intrinsic factors include herd susceptibility, infection and immunity etc., which change over time through the normal processes of disease transmission. The extrinsic factors are often due to climate, which affects the average amount of transmission in any area, and weather which influences its seasonality. Biological models should describe the intrinsic factors well, but will be rendered more or less inaccurate by the extrinsic factors, unless they are explicitly included. Statistical models exploit the relationships of case numbers to these extrinsic factors, but are unable to cope with the intrinsic factors easily. Thus, what is the 'signal' for one approach is the statistical 'noise' of the other. Biological models tend to cope with their statistical noise by drawing demographic parameters from predefined frequency distributions that may or may not be linked to seasonality: statistical models cope with their noise by introducing spatial or temporal autoregressive terms that patently acknowledge, in a rather ill-defined way, the biological fact that present case numbers depend on nearby, or past, case numbers. We believe that progress will be made in this field by combining the best of the statistical and biological approaches, and warn against the exclusive use of one or the other. Many examples of this epidemiological 'exploration' process are reviewed by Rogers (this volume), Hay *et al.* (this volume), Randolph (this volume) and Brooker and Michael (this volume).

Developing an appropriate model is one of the most crucial steps in determining the robustness of any early warning system and is discussed with respect to malaria early warning systems (MEWS) in Africa (Hay *et al.* 2000a). Africa displays considerable spatial heterogeneity in its climate and ecology (see Plate 16). It follows that malaria distribution will reflect this environmental heterogeneity in space and in time. Without elaborating the quantitative epidemiology (Hay *et al.*, 2000a), it is plain that in extremely arid areas malaria will be limited by rainfall, which provides habitats in which mosquitoes can oviposit. For example, the relationship between malaria cases and rainfall in Wajir, a town in the arid north of Kenya, is shown in Plate 17. Positive rainfall anomalies in Wajir are a good indicator of malaria cases 3 months into the future; the lag presumably reflects the time for the mosquito population to establish. Following on from this, a system to monitor rainfall anomalies for the arid and semi-arid areas of Africa is shown in Plate 18. It is particularly important to monitor these arid areas, because the usual lack of malaria means that the population has little immunity to the disease and is therefore very susceptible to infection. Epidemics in these areas can have a devastating impact across all age groups (Brown *et al.*, 1998). Satellite sensors can provide timely remotely sensed data on which to base such monitoring systems (Hay *et al.*, 1996, 1997; Hay, 1997; Hay, this volume).

Similarly, positive temperature anomalies in cold areas (usually at high elevation in Africa) can be reliable predictors of malaria, since low temperatures normally limit parasite development within the vectors. Thus simple systems to monitor temperature anomalies could be important for 'epidemic' warning in these locations.

In more endemic malaria areas, such as Kericho in western Kenya, human and parasite population dynamic effects complicate relationships between malaria cases and climate. Malaria is always present, so children who survive to adulthood develop a functional immunity and epidemics can only occur when the non-immune population has grown, through recovery, births and immigration (Shanks *et al.*, 2000). Climate therefore acts in

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concert with the population dynamics of malaria in endemic areas (Hay *et al.*, 2000b) and will have to be considered when developing MEWS for such zones.

The above contrasts show some of the complexity inherent in developing a predictive malaria model. A single biological model should be capable of describing all malarious situations, but is not yet available because the interaction between extrinsic and intrinsic factors in the expression of malaria is not completely understood. For the time being, therefore, we are left with several (location-specific) statistical models.

2.2.3. Component 3: Disease Forecasting and Prediction—At the heart of early warning is a basic trade-off between the specificity of predictions (in space and time) and the lead times which those predictions can provide. In general, long-range forecasts give the least specific warnings, but have the advantage of providing planners with relatively long lead times. At the other extreme, systems based on early detection of cases provide highly specific information on the timing and location of outbreaks, but allow little time for implementing remedial measures. Any prediction of risk should include an estimate of its reliability (Frisén, 1992). This is particularly important from a health-planning standpoint, as resources will only be mobilized once a 'critical level' of confidence has been exceeded. While some elements of intervention (such as allocating extra resources within health budgets) may require relatively low confidence predictions, other activities may only proceed once more specific predictions are available (and the danger of a false alarm is less likely).

Epidemic prevention and control activities usually involve a chain of events and it is important to recognize the potential usefulness of a wide range of indicators, which may be combined to create an integrated prediction strategy. Such a hierarchical system has recently been proposed for tracking malaria epidemics in highland areas of Africa (Cox *et al.*, 1999). It combines elements of long and medium range forecasting as well as the early detection of malaria outbreaks through direct epidemiological surveillance (see Figure 1). These elements provide warning signals that can be thought of as a series of 'flags', which correspond to increasing degrees of alarm, and trigger activities of increasing degrees of urgency. Each flag relates to a specific set of indicators, and leads to a specific set of responses following predefined procedures. These responses also anticipate the next level of indicators with an increased sensitivity. As shown in Figure 1, successive flags carry increasing weight. From a planning perspective, it is important that the higher weight flags are implemented first.

3. TYPES OF EARLY WARNING SYSTEM

The criteria for selection of any EWS are: the information requirements of the health community; the scale of analysis (i.e. local, regional, national); and the technological requirements for modelling or prediction. EWSs comprise one or more of the following types of activity: (i) reportorial, involving collected reports of outbreaks from health care professionals; (ii) risk maps or indicators based on seasonality or changes in environment of the vector; (iii) threshold alerts indicating changes in acceptable ranges derived from ongoing surveillance systems; and (iv) EWSs modelled from ongoing disease surveillance and operational environmental monitoring of sentinel sites.

3.1. Reportorial Systems

Formal and informal systems provide case data for reporting and investigation. Formal networks include the US CDC, the UK Public Health Services, the French Instituts Pasteur and the Training in Epidemiology and Public Health Network, among others (Parsons *et al.*, 1996). These networks provide laboratory-confirmed reports of outbreaks of new diseases

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and shifts in patterns of endemic ones (Bryan *et al.*, 1994; Berkelman, 1998). Most are, or will become, part of the WHO Collaborating Centre network (Heymann and Rodier, 1998). While falling primarily under the category of early detection, there is also potential within this system for providing long-range risk forecasting of disease events by expert surveillance and laboratory confirmation.

Informal networks may be national, such as SentiWeb, or regional, such as the Pacific Network (PacNet). Important informal networks include the Program for Monitoring Emerging Diseases (ProMed) that provides open postings of outbreaks of both familiar and new diseases to 18 000 subscribers in 150 countries via email (Chase, 1996). The Global Public Health Information Network (GPHIN), meanwhile actively trawls the Internet looking for reports of communicable diseases in news groups, wire service postings and other listings, and reports its findings to WHO for response and verification (Cribb, 1998).

While remote sensing is used little, if at all, in reportorial systems, high-resolution satellite imaging can be an important tool for increasing the efficiency of notification of population networks, particularly for emerging problems in unmapped areas. The use of remote sensing for population surveillance may see greater use in reportorial systems as WHO implements a strategy of geographically identified surveillance centres and ProMed develops its proposal of selected surveillance centres for monitoring responsibilities (FAS, 1999).

3.2. Risk Mapping Systems

Disease data, however collected, may be turned into static maps of risk. They may also be used to develop new statistical approaches to risk mapping, to test the association of weather anomalies with disease outbreaks and to test biological models that give rise to risk predictions. This sequence is one of increasing complexity, and therefore increasing uncertainty. Each of the many links in the chain of causation must be accurately described before a biologically based model can accurately describe disease risk through both space and time.

3.2.1. Static Risk Maps—Mapping hot spots for disease was one of the earliest methods to identify risk areas for epidemiology. As discussed earlier, Rogers (1923, 1925a,b, 1926) and Gill (1921, 1923) were able to use historic environmental and epidemiological data to develop risk maps for a wide variety of diseases in the first quarter of the twentieth century; these maps were subsequently used for decades. Risk maps of malaria in Africa were developed by experts beginning in the 1950s (Hay *et al.*, 1998) and their production is among the primary aim of the Mapping Malaria Risk in Africa/Atlas du Risque de la Malaria en Afrique (MARA/ARMA) collaboration (Hay *et al.*, this volume). Data collation within a geographical information system (GIS) will identify disease hot spots and these may be targeted for long-term control. No further attempt need be made to understand the reasons for the hot spots in the first place: like a fire risk map, a static disease risk map tells us where, and perhaps when, to expect an outbreak, but not why.

3.2.2. Statistical Risk Maps—The GIS disease data may be related to ancillary data, such as satellite sensor information, soil and water types, human agricultural activities etc., using a variety of regression or maximum likelihood methods (Curran *et al.*, this volume; Robinson, this volume; Rogers, this volume). The relationships established between the predictor (e.g. satellite) and the predicted (e.g. disease) data may then be used to predict risk in previously unsurveyed areas. Seasonally varying satellite data may also be used to describe seasonally varying risk. Anomalies from the usual patterns of satellite data in both space and time can be associated with varying risks, to improve the accuracy of short-term risk map forecasts.

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Just as statistical analysis may be used to predict spatial variation in risk, so different sorts of statistical analyses can predict variation through time. A whole variety of time series analytical methods is available, from spectral analysis to autoregression methods (Chatfield, 1975; Diggle, 1990). It is possible to show the fundamental similarities between many of these techniques. As outlined in the introduction to this section, it is assumed that patterns in past data can be projected into the future to make predictions of future case numbers. Uptake of such systems will depend upon both the reliability of such forecasts and the lead time they give for sensible mitigating responses. One example of this approach is the development of a dengue early warning system by NASA's Inter-agency Research Partnership for Infectious Diseases (IntRePID).

IntRePID began life as a US federal agency working group in 1996, investigating whether technologies and data from NASA's suite of earth observing satellites could be applied to the development of early warning systems for infectious diseases. The dengue early warning system (DEWS) is a prototype system which is undergoing testing to validate the accuracy of the predictions in real-time. The prototype is designed to receive data from Bangkok and the four main regions of Thailand and is based on previous Thai systems for malaria 'epidemic' surveillance (Cullen *et al.*, 1984) and responds to calls for such a facility (Gunakasem *et al.*, 1981). When fully validated, the system will form an international EWS for dengue. The system comprises several models.

The surveillance model allows new case data to be compared against the long-term average case data. As additional disease data are received they are plotted against the long-term average for that month. The user is then able to determine the severity of the current outbreak against historical conditions. The line of two standard deviations above the long-term mean is also drawn to help with this comparison: if cases exceed two standard deviations from the normal, there is significant cause for concern. This is flag 3 of Figure 1.

The DEWS risk map module, again using Thailand as a prototype, displays historical records from separate administrative units (i.e. changwats) to show the spatial distribution of dengue cases on a national basis from 1982 to 1997. These data refer to relatively severe cases requiring a visit to a local clinic or hospital, although it is not possible to distinguish in them severe dengue from dengue haemorrhagic fever. Estimated populations over the same period of time, are used to turn disease cases into disease incidence per 100 000 population. Incidence was related to National Oceanic and Atmospheric Administration (NOAA) Advanced Very High Resolution Radiometer (AVHRR) satellite data using maximum likelihood methods, and the full resolution satellite data were used to produce country-wide risk maps. The analysis helps to identify crucial environmental variables determining local variation in risk, and the risk maps may be updated in near real time as recent satellite data are incorporated into the risk map model.

The DEWS forecasting module is based on a time-series analysis of past case numbers of this disease. It was initially developed for Bangkok, followed by the four main regions of Thailand (the north, northeast, central and southern regions). Inspection of monthly case data over many years shows that there are not only within-year cycles of variation in dengue in Bangkok, but considerable between-year variation as well. Temporal Fourier analysis (Rogers, this volume) of the de-trended time series splits the case data into a series of regular cycles (the 'harmonics') with frequencies ranging from one complete cycle every 2 months to one complete cycle only once in the entire duration of the records. The between-year cycles are included without modification in the model predictions. To these are added both a fitted trend line and a description of within-year variation. The latter are predicted from relationships established between monthly temperature and the within-year residuals 4 months later; biologically this implies that annual temperature changes trigger a series of

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processes that result in changing case numbers in the future, with a peak at the 4 month mark.

The descriptive skill of this model is excellent, with past dengue records being described with acceptable accuracy. The three components of the model can also be projected into the future to make disease predictions. The first two component projections are based on extending the trend or between-year harmonics and the third uses the observed mean monthly temperatures for previous years. These predictions are reasonably good for non epidemic years, but are not yet able to capture the full extent of epidemic cycles which occur irregularly.

3.2.3. Anomaly Risk Maps—There is increasing evidence that longer term climatic events, such as the aperiodic El Niño southern oscillation (ENSO) that affect local patterns of rainfall, have some impact on vector-borne diseases (among others, Nicholls 1993; Bouma *et al.*, 1997; Baylis *et al.*, 1999; Maelzer *et al.*, 1999). The effect of El Niño on local rainfall varies spatially; in some places rainfall increases, in others it decreases. The effect also varies temporally; some El Niños cause an increase in local rainfall, others a decrease in the same areas, and disease outbreaks may only be associated with one of these changes (Baylis *et al.*, 1999). Our ability to detect the early signs of developing El Niño conditions has increased dramatically in recent years. If we could be confident of predicting the climatic consequences of these events, El Niño-associated disease outbreaks could be anticipated and mapped.

Factors intrinsic to the disease system can also generate periodic outbreaks, however, and these may be difficult to distinguish from extrinsically driven cycles. There is strong evidence that these intrinsic cycles have periods approaching, but not quite matching, those of El Niño (Hay *et al.*, 2000b). Teasing apart the intrinsic and extrinsic influences in such cases is technically difficult, and remains controversial.

3.2.4. Biological Risk Maps—These maps exploit what is known about the biological relationships between organisms in the period leading up to disease outbreaks. In many cases a particular event, or chain of events, triggers an eventual outbreak of disease.

(a) Hantavirus Pulmonary Syndrome: Glass *et al.* (2000) uses Landsat thematic mapper (TM) data to establish annual risk predictions for hantavirus pulmonary syndrome (HPS). This is a disease of humans caused by infection with members of the viral genus *Hantavirus*, which are carried in the US by certain native rodent species (Engelthaler *et al.*, 1999). The disease was first recognized in the US in 1993, following the 1991–1992 El Niño event. The presumptive chain of events leading to the original outbreak involves increased precipitation during the winter and spring, leading to increased vegetation and insect population growth, which in turn provide food and shelter for the rodent reservoirs. When climatic conditions return to normal, vegetation growth declines, forcing the rodents into human habitation in search of food and shelter. This leads to increased contact with humans and transmission of the hantavirus. The entire sequence has been termed the ‘trophic cascade hypothesis’ (TCH), and is currently being tested (Glass *et al.*, 2000).

Surveillance of HPS is based on the assumption that environmental conditions favouring the rodents precede, by a substantial time, the increase in rodent populations and their subsequent movement into houses. To generate an efficient surveillance algorithm, locations where cases of disease occurred in 1993 were compared with locations where people had not contracted HPS. Positive sites were characterized using Landsat-TM data and these characteristics were used to evaluate risk for the subsequent year for each pixel in a 105 000 km^2 region. Areas of high, medium and low risk were defined. The algorithm predicted the

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extent and timing of HPS risk in 1994, 1996, 1998, and 1999 using satellite imagery from each of the preceding years. More than 90% of cases in these years occurred in the predicted medium to high risk areas. Risk maps are now produced annually in conjunction with the American Indian Health Service.

(b) Nasal Bot Fly: The nasal bot fly, *Oestrus ovis*, is an insect pest of livestock in Namibia. It develops at shallow depths in the soil and the timing of its emergence is directly dependent on the number of degree days, i.e. the summed product of soil temperatures above a developmental threshold and the time over which they apply (Flasse *et al.*, 1998). Meteosat satellite sensor imagery provides accumulated soil temperature information to identify trigger conditions conducive to outbreaks and provides a broader warning capability than ground surveillance alone.

(c) Rift Valley Fever: Recent work has identified a complex relationship between Rift Valley fever (RVF) in Kenya with sea surface temperature change in the Indian Ocean (Linthicum *et al.*, 1999). RVF affects domestic animals and humans throughout Africa and results in widespread livestock losses and frequent human mortality. Virus outbreaks in East Africa, from 1950 to May 1998, followed periods of abnormally high rainfall, and previous work used Normalized Difference Vegetation Index (NDVI) data derived from the NOAA-AVHRR to detect conditions associated with the earliest stages of an RVF epizootic (Linthicum *et al.*, 1987, 1990). Identification of potential outbreak areas was refined using higher resolution Landsat-TM, Satellite pour l'Observation de la Terre (SPOT), and air-borne Synthetic Aperture Radar data to identify mosquito habitats. By incorporating both Pacific and Indian Ocean sea surface temperature anomaly data together, recent studies have successfully predicted each of the three RVF outbreaks that occurred between 1982 and 1998, without predicting any false RVF events (Linthicum *et al.*, 1999).

(d) Dengue and Dengue Haemorrhagic Fever: Focks *et al.* (1995) have developed a two-part predictive model for dengue that incorporates entomological and human population data with weather data. The two parts are named CIMSiM (container-inhabiting mosquito simulation model) and DENSiM (dengue simulation model). The entomological model (CIMSiM) is a dynamic life-table simulation model that produces mean-value daily estimates of various parameters for all cohorts of a single species of *Aedes* mosquito within a representative 1-hectare area. The model takes account of breeding container type and its relative abundance in the environment, and predicts adult production from these variables. Because microclimate is an essential determinant of survival and development for all stages, CIMSiM also contains an extensive database of daily weather information.

DENSiM is essentially the corresponding account of the dynamics of a human population driven by country- and age-specific birth and death rates. The entomological variables output from CIMSiM are input into DENSiM, which follows the individual infection history of the modelled human population.

Parameters estimated by DENSiM include demographic, entomological, serological, and infection information on a human age group and/or time basis. As in the case of CIMSiM, DENSiM is a stochastic model. The DENSiM/CIMSiM model combination has been validated in many locations and is currently being used to model dengue risk in Brownsville, New Orleans and Puerto Rico.

3.2.5. Developing a Global Mapping Capability—The joint WHO/UNICEF programme HealthMap is a data management, mapping and GIS system for public health. Initially created in 1993, HealthMap was initiated to support management and monitoring of the Guinea Worm Eradication Programme (GWEP). Since 1995, it has grown in response to

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the increasing demand to include mapping and GIS activities for other disease control programmes, including malaria, onchocerciasis, African trypanosomiasis and lymphatic filariasis (HealthMap, 2000).

Maps for the GWEP combine village-level epidemiological maps with entomological data maps to track and visualize local prevalence trends, dependencies such as access to health resources, and social infrastructures. The system today incorporates more socioeconomic and environmental variables to provide a broader-access mapping display designed to enable policy makers to target scarce resources better at communities at greatest risk. HealthMap archives historical data and can be considered to provide predictive data through its trending information displays. As part of the WHO international programme Roll Back Malaria, HealthMap is developing relational geo-referenced databases to determine the various types of malaria transmission. These use global positioning systems, ground and satellite sensor information, including rainfall, elevation and temperature, and epidemiological data. The maps will serve as an operational tool for planning and target control interventions including bed nets and spray operations (HealthMap, 2000).

3.3. Threshold Alert Systems

These systems are based on time series of surveillance data and were discussed in Section 2.2.1.

3.4. Environmental Early Warning Systems

The objective of a forecasting system is to predict the future course of disease case numbers, giving health care workers sufficient warning for them to deal with unexpectedly high (or low) case numbers, or else to implement control measures to prevent disease outbreaks from happening in the first place. In general, epidemic forecasting is most useful to health services when it predicts case numbers 2 to 6 months into the future, allowing tactical responses to be made when disease risk is predicted to increase. Longer-term forecasting is required when strategic control of diseases is the objective (e.g. as in WHO's Onchocerciasis Control Programme to reduce river blindness in parts of West Africa), something which is possible only with a very clear understanding of the transmission dynamics of the disease being controlled. Both spatial and temporal changes in environmental conditions may be important determinants of vector-borne disease transmission.

4. CONCLUSIONS: WHAT MAKES A GOOD PREDICTION?

Several factors can be identified as important components in establishing a good prediction for risk of epidemic or disease. Primary among these are the accuracy of prediction, as well its geographical scale and temporal duration. Processes that should be incorporated into EWS implementation include broad validation of the model, application of models at scales appropriate to public health managers, and regular reassessment of data reliability, all coupled with expert review. Predictions should be linked with response initiatives so that they can be updated based on these actions. In this way, officials responsible for containing an outbreak can determine the reliability of predictions, the effectiveness of their responses and the level of effort required for an ongoing outbreak. Further issues include international cooperation in sharing sometimes sensitive surveillance data, as well as the burden of prediction validation.

The previous experiences of the famine EWS suggests that the impact of the system is often less related to the accuracy of the prediction, than to the fact that EWS information is not routinely used by the relevant decision makers. There were many, principally related to

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political and institutional factors and to logistical obstacles to launching adequate, timely response (Buchanan-Smith and Downing, 1995; Buchanan-Smith, 1996). These authors found that the international relief system 'responds to famine once it is underway but is ill-equipped to provide genuinely *early* warning'. This situation will not simply be changed by proving that an EWS is reliable. If policy-makers cannot easily determine the human or economic value of an early warning, the likelihood of implementation is small. Information therefore needs to be provided in a way that can be easily interpreted and in such a way that it influences the decision making process. These are areas that require investigation and forethought.

Acknowledgments

The authors would like to acknowledge the generous support of the National Aeronautics and Space Administration's Earth Science Enterprise Environment & Health Initiative and The Innovation Fund of the National Performance Review, whose support for the Interagency Partnership for Infectious Diseases (INTREPID) made this review possible. We are also grateful to Bob Snow and Sarah Randolph for comments on this manuscript. SIH is an Advanced Training Fellow funded by the Wellcome Trust (No. 056642).

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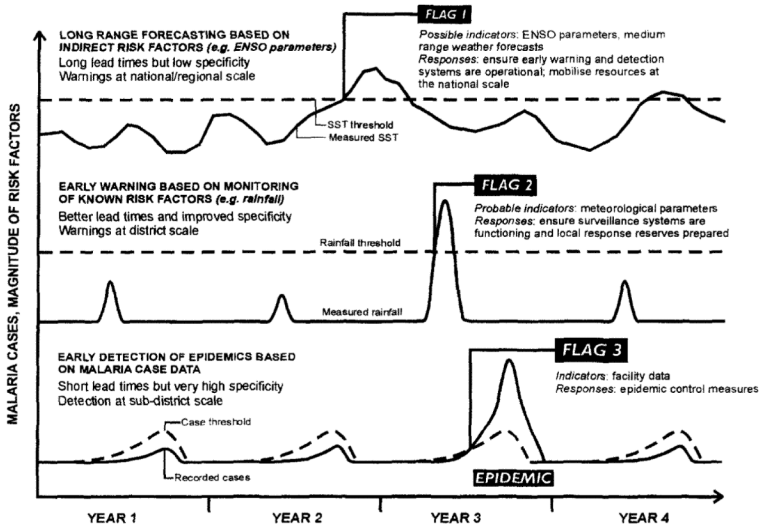
LONG RANGE FORECASTING BASED ON INDIRECT RISK FACTORS (e.g. ENSO parameters)
Long lead times but low specificity
Warnings at national/regional scale
FLAG 1
Possible indicators: ENSO parameters, medium range weather forecasts
Responses: ensure early warning and detection systems are operational; mobilise resources at the national scale
SST threshold
Measured SST
EARLY WARNING BASED ON MONITORING OF KNOWN RISK FACTORS (e.g. rainfall)
Better lead times and improved specificity
Warnings at district scale
FLAG 2
Probable indicators: meteorological parameters
Responses: ensure surveillance systems are functioning and local response reserves prepared
Rainfall threshold
Measured rainfall
EARLY DETECTION OF EPIDEMICS BASED ON MALARIA CASE DATA
Short lead times but very high specificity
Detection at sub-district scale
FLAG 3
Indicators: facility data
Responses: epidemic control measures
Case threshold
Recorded cases
EPIDEMIC
MALARIA CASES, MAGNITUDE OF RISK FACTORS
YEAR 1
YEAR 2
YEAR 3
YEAR 4

Figure 1.

A three-tiered approach for epidemic forecasting, early warning and detection. Each tier is associated with specific indicators and responses. In this simplified example for malaria epidemics, a first warning flag is raised at the regional level after Sea Surface Temperature (SST) anomalies suggest an impending El Niño event. Subsequent excess rainfall is monitored directly as part of an early warning system and Flag 2 is raised once a critical threshold is reached. Malaria cases are monitored at the individual (sentinel) facility level and an epidemic declared once a defined threshold has been reached. (Cox *et al.*, 1999).

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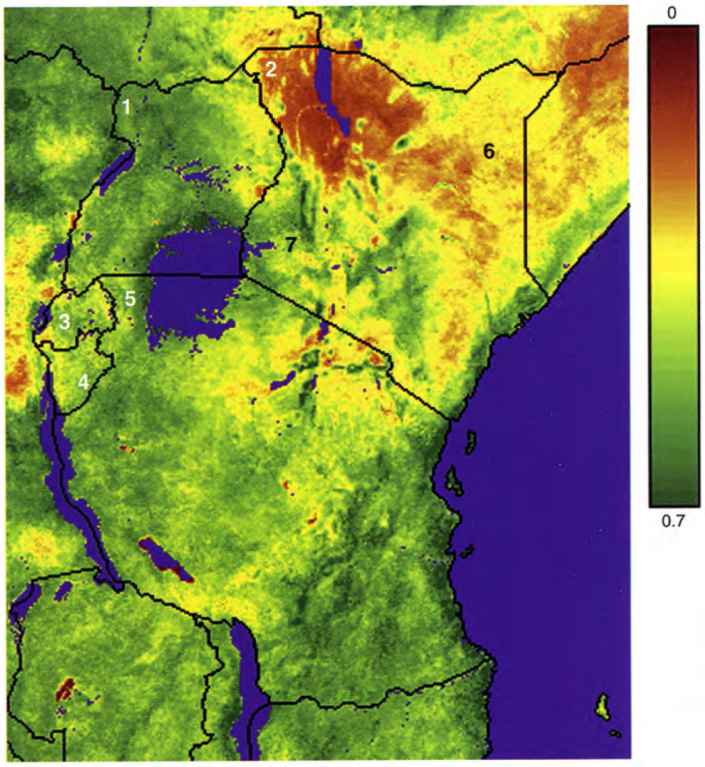

Plate 16.
Average Normalized Difference Vegetation Index (NDVI) of East Africa during 1993 at a 1 × 1 km spatial resolution. The image is based on daily retrievals from channels 1 and 2 of the AVHRR on the National Oceanic and Atmospheric Administration (NOAA) satellites. The NDVI is scaled linearly between brown (0) and green (0.7). Blue indicates permanent water, and north is to the top of the page. The white numbers represent the following countries: 1, Uganda; 2, Kenya; 3, Rwanda; 4, Burundi; 5, Tanzania. The black numbers 6 and 7 indicate the location of Wajir and Kericho, respectively, whose malaria epidemiology is contrasted in the text. See Myers et al. (this volume).

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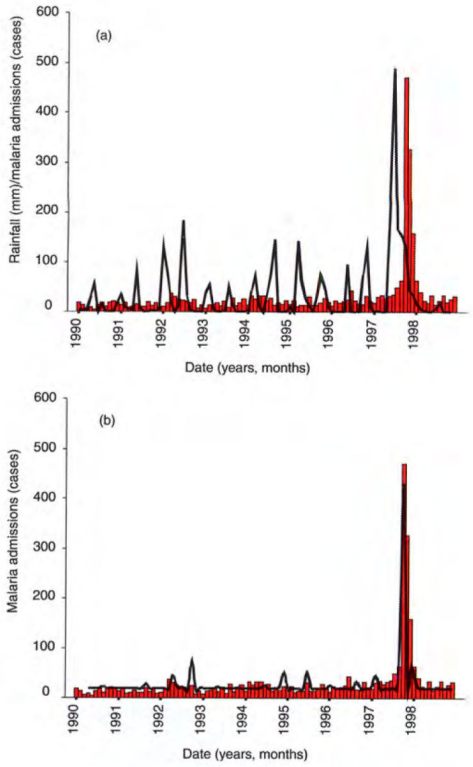

Plate 17.

(a) Malaria cases and rainfall by month (1991–1998) for Wajir, Northern Kenya. Red bars indicate malaria cases, and black lines rainfall totals. (b) Observed (red bars) and predicted (black line) malaria cases in Wajir, Northern Kenya. The prediction is based on a simple quadratic relationship between present cases (x) and rainfall (y) 3 months previously; where $x = 19.9635 - 0.0399y, + 0.0018y^2$. The 20-case baseline is a statistical artefact, probably resulting from the background of imported malaria cases. See Myers *et al.* (this volume).

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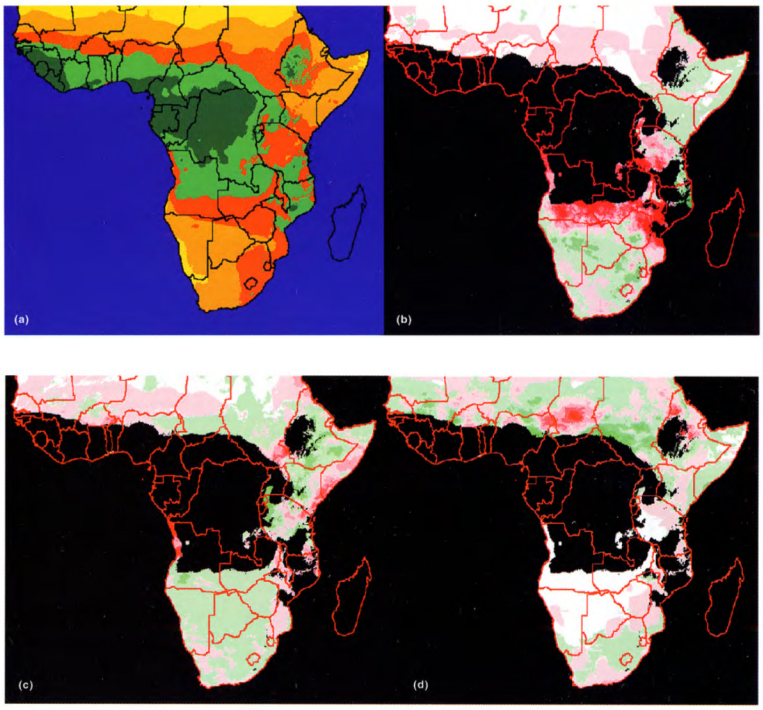

Plate 18.
Rainfall anomalies in the arid areas of sub-Saharan Africa. (a) An ecological classification for Africa based on rainfall amount (Pratt and Gwynne, 1977) using long-term climate data (Hutchinson *et al.*, 1995). Yellow corresponds to deserts, and light and dark orange to arid and semi-arid regions, respectively. The light- and dark-green areas are sub-humid and humid zones, which are masked out of the other maps in this plate. (h) Rainfall anomaly maps for January 1999 calculated as deviations from the long-term average. Red areas indicate negative deviations, white no change and green positive deviations, and the data are scaled linearly between the darkest red (−200 mm) and the darkest green (+200 mm) areas. In all maps, north is to the top of the page, and data for Madagascar are not shown. See Myers *et al.* (this volume). Rainfall anomalies in the arid areas of sub-Saharan Africa. (c)–(d) Rainfall anomaly maps for April and July 1999, respectively, calculated as deviations from the long-term average. Red areas indicate negative deviations, white no change and green positive deviations, and the data are scaled linearly between the darkest red (−200 mm) and the darkest green (+200 mm) areas. In all maps, north is to the top of the page, and data for Madagascar are not shown. See Myers *et al.* (this volume).

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